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(12) **United States Patent**
Mullan(10) **Patent No.:** **US 7,538,258 B2**
(45) **Date of Patent:** **May 26, 2009**(54) **TRANSGENIC MOUSE EXPRESSING AN APP 670/671 MUTATION**(75) Inventor: **Michael John Mullan**, Tampa Palms, FL (US)(73) Assignee: **Alzheimer's Institute of America, Inc.**, Mission Hills, KS (US)

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(51) **Int. Cl.****A01K 67/033** (2006.01)**G01N 33/00** (2006.01)(52) **U.S. Cl.** **800/12; 800/18; 800/3**(58) **Field of Classification Search** None
See application file for complete search history.(56) **References Cited****U.S. PATENT DOCUMENTS**

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Higgins et al. Transgenic mice expressing human beta-APP751, but not mice expressing beta-APP695, display early Alzheimer's disease-like histopathology. *Annals NY Acad. Sci.* 1993, vol. 695, pp. 224-227.*Felsenstein et al. Transgenic Rat and In-Vitro Studies of β -Amyloid Precursor Protein Processing. Hanin, I. et al., eds., *Advances in Behavioral Biology: Alzheimer's and Parkinson's diseases: Recent developments*. Publisher: Plenum Press, 1995, pp. 401-405.*Kappel et al (1992) Regulating Gene Expression in Transgenic Animals, *Current Opinion in Biotechnology*, vol. 3, 548-553.*Andra et al. "Expression of APP in Transgenic Mice: A Comparison of Neuron-Specific Promoters." *Neurobiol. Aging* 17(2):183-190 (1996).*Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education* 304 F.3d 1221, 1220-1235 (Fed. Cir. 2002).Forss-Petter et al. "Transgenic Mice Expressing β -Galactosidase in Mature Neurons under Neuron-Specific Enolase Promoter Control." *Neuron* 5:187-197 (1990).Felsenstein, et al., "Transgenic Rat and In-Vitro Studies of β -Amyloid Precursor Protein Processing. Hanin, I. et al., eds., *Advances in Behavioral Biology: Alzheimer's and Parkinson's diseases: Recent developments*." Publisher: *Plenum Press*, pp. 401-405 (1995).Greenberg et al. "APP Transgenesis: Approaches Toward the Development of Animal Models for Alzheimer Disease Neuropathology." *Neurobiol. Aging* 17(2):153-171 (1996).Higgins, et al., "Transgenic mice expressing human β -APP751, but not mice expressing β -APP695, display early Alzheimer's disease-like histopathology." *Annals NY Acad. Sci.* 695:224-227 (1993).Hsiao et al. "Correlative Memory Deficits, A β Elevation, and Amyloid Plaques in Transgenic Mice." *Science* 274:99-102 (1996).Hsiao et al. "Measuring Memory in a Mouse Model of Alzheimer's Disease." *Science* 277:839-841 (1997).Kappel, et al., Regulating Gene Expression in Transgenic Animals, *Current Opinion in Biotechnology* 3:548-553 (1992).Lannfelt, et al., "Alzheimer's Disease: Molecular Genetics and Transgenic Animal Models." *Behav. Brain Res.*, 57:207-213 (1993).Malherbe et al. "Lack of β -Amyloidosis in Transgenic Mice Expressing Low Levels of Familial Alzheimer's Disease Missense Mutations." *Neurobiol. Aging* 17(2):206-214 (1996).Selkoe, D., "In the Beginning . . ." *Nature*, 354:432-433 (1991).Sturchler-Pierrat et al. "Two amyloid precursor protein transgenic mouse models with Alzheimer disease-like pathology." *Proc. Natl. Acad. Sci. USA* 94:13287-13292 (1997).Yehiely et al. "Identification of Candidate Proteins Binding to Prion Protein." *Neurobiol. Disease* 3:339-355 (1997).Zhao et al. " β -Secretase Processing of the β -Amyloid Precursor Protein in Transgenic Mice is Efficient in Neurons but Inefficient in Astrocytes." *J. Biological Chem* 271(49):31407-31411 (1996).

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The invention provides an isolated nucleic acid characteristic of human amyloid precursor protein 770 including the nucleotides encoding codon 670 and 671, wherein the nucleic acid encodes an amino acid other than lysine at codon 670 and/or an amino acid other than methionine at codon 671. Also provided is a method of diagnosing or predicting a predisposition to Alzheimer's disease, comprising detecting in a sample from a subject the presence of a mutation at a nucleotide position corresponding to codons 670 and/or 671 of amyloid precursor protein or fragment thereof, the presence of the mutation indicating the presence of or a predisposition to Alzheimer's disease.

6 Claims, 1 Drawing Sheet